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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/650,791	08/29/2003	Roy L. Ax	240523US20	3674

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EXAMINER	
GRUN, JAMES LESLIE	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 10/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/650,791	AX ET AL.	
	Examiner	Art Unit	
	James L. Grun	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-54* is/are pending in the application.

4a) Of the above claim(s) *1-28,34,35,42 and 54* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29-33,36-41 and 43-53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-54* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *08/06/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Applicant's election with traverse of Group II, claims 29-33, 36-41, and 43-53 in the paper filed 12 July 2006 is acknowledged. The traversal is on the ground(s) that adequate reasons have not been provided to support patentable distinctness between the groups, particularly groups I and II. This is not found persuasive for the reasons of record because the explanations of different structures, functions, classifications, materially different uses, and/or fields of search made in the restriction requirement of record are sufficient to provide a *prima facie* showing of a serious burden upon the examiner. Although the searches for an antibody and a method of determining fertility may be overlapping, they are clearly not co-extensive.

The requirement is still deemed proper and is therefore made FINAL.

The disclosure is objected to because of the following informalities: at page 4, the listing of humans as "livestock" is repugnant to the art; at page 10, the sequence disclosed in Fig. 8 should be identified as a fragment of SEQ ID NO: 4. Appropriate correction is required.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention, and failing to adequately teach how to make and/or use the invention, i.e. failing to provide an enabling disclosure.

Claims 29-33, 36-41, and 43-53 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, particularly the invention commensurate in scope with these claims.

Claims 29, 31-33, 36, 38-41, 43, and 45-53 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, particularly the invention commensurate in scope with these claims.

Applicant teaches a polyclonal antibody elicited to a recombinant fragment consisting of amino acid residues 73-269 of SEQ ID NO: 2, a fragment of the protein identified as the approximately 30kDa heparin binding protein in bovine seminal fluid with sequence similarity to a human DNase-I-like protein (see Zhang et al. (US 6,891,029)). The presence of a protein immunoreactive with this antibody population in bull semen appears to correlate with an increase in the fertility of these bulls (see e.g. Example 4, pages 37-39). These results are in accord with previous results indicating that the presence of heparin binding proteins, of which the identified protein is a member, correlate with an increase in the fertility of bulls (see e.g. Ax et al. (US 5,962,241)). Applicant discloses no other protein or antibody thereto which functions predictably in the method. Undue experimentation, unguided by applicant's disclosure, would be required to determine other proteins and antibodies binding thereto which function in the invention other than those antibodies binding to the protein having SEQ ID NO: 2.

Moreover, the presence of proteins immunoreactive with the antibody preparation were also demonstrated on sperm of other animal species. However, there is nothing in evidence to correlate the presence of immunoreactive proteins in the sperm or semen of other species with any measure of the degree of fertility of the sperm. As is well known in the art, "the biological effect of heparin on sperm physiology is not conserved among mammalian species" (Calvete et al., FEBS Lett. 399: 147, 1996, see page 150, col. 2). In this regard, in contrast to the results in bulls, heparin binding of human sperm was generally inversely correlated with semen quality (see e.g. Carrell et al. (Arch. Androl. 48: 147, 2002)). Similarly, DNase activity was lower in normospermic than in oligozoospermic human semen samples (Singer et al., Arch. Androl. 15: 105, 1985). Thus, absent further guidance from applicant, one would have no assurance of the ability to successfully practice the method as disclosed and claimed, to detect a heparin binding DNase as indicative of fertility, with other than bull semen samples.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 29-33, 36-41, and 43-53 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 29 and claims dependent thereupon, essential steps are ommitted, such omission amounting to a gap between the steps. For example, it is not clear how one assays or quantifies merely by contacting sample with antibody. In these claims, "the" presence lacks antecedent basis.

In claims 32 and 33, "the amount of binding activity" lacks antecedent basis.

In claim 36 and claims dependent thereupon, essential steps are ommitted, such omission amounting to a gap between the steps. For example, it is not clear what interaction is detected or how this relates to assessing fertility. In these claims, "the" fertility lacks antecedent basis.

In claim 40, "the amount of binding activity" and "the relative presence" lack antecedent basis. It is also not clear what the presence is relative to or how one determines the degree of being relative.

In claim 41, "the" donor or group lack antecedent basis. It is believed that dependency from claim 40 was intended.

In claim 43 and claims dependent thereupon, essential steps are ommitted, such omission amounting to a gap between the steps. For example, it is not clear how one assays or quantifies merely by contacting sample with antibody. In these claims, "the" presence lacks antecedent basis.

In claims 46 and 47, "the amount of binding activity" lacks antecedent basis.

In claim 48 and claims dependent thereupon, essential steps are ommitted, such omission amounting to a gap between the steps. For example, it is not clear what interaction is detected or how this relates to assessing fertility. In these claims, "the" fertility lacks antecedent basis.

In claim 52, "the amount of binding activity" and "the relative presence" lack antecedent basis. It is also not clear what the presence is relative to or how one determines the degree of being relative.

In claim 53, "the" donor or group lack antecedent basis. It is believed that dependency from claim 52 was intended.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 29, 30, 32, 33, 36, 37, 39, 40, 41, 43, 44, 46-49, and 51-53 are rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Cancel et al. (Biol. Reprod. 57: 1293, 1997).

Cancel et al. elicited polyclonal antibodies to a fertility associated protein, reacted seminal plasma samples of bulls with the antibodies, and correlated the level of binding with bull fertility (see e.g. Fig. 1).

Claims 29, 30, 36, 37, 39, 43, 44, 48, 49, and 51 are rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Gerena et al. (Biol. Reprod. 58: 826, 1998).

Gerena et al. elicited polyclonal antibodies to a fertility associated protein, reacted seminal plasma samples of bulls with the antibodies, and determined the presence of binding.

Claims 29-31, 36-39, 43-45, and 48-51 are rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Leblond et al. (Mol. Reprod. Dev. 34: 443, 1993).

Leblond et al. elicited polyclonal antibodies to fertility associated proteins, reacted seminal plasma samples of bulls, humans, and other species with the antibodies, and determined the presence of binding.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
> (c) Subject matter developed by another person, which qualifies as prior art only under one or more subsections (e), (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.
>
> This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

Claims 29-33, 36-41, and 43-53 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Ax et al. (US 5,962,241) in view of McCauley (Mol. Reprod. Dev. 54: 145, 1999), Tanuma (EP 1,094,080) and Yoshihara et al. (Biochem. Biophys. Res. Comm. 236: 423, 1997).

Ax et al. teach the determination of fertility by the immunoassay detection of heparin binding proteins, particularly the protein of approximately 30kDa, in a sample of semen. Although antiserum from the mouse used for the fusion to produce a monoclonal antibody was tested in binding assays, in contrast to the invention as instantly claimed, the reference does not teach the use of this or another polyclonal antibody and teaches a monoclonal antibody which cross-reacts with a number of the heparin binding proteins in the assay for fertility determination.

McCauley et al. teach the identification of the approximately 30kDa heparin binding protein in bovine seminal fluid as a DNase-I-like protein with sequence similarity to the human DNase-I-like enzyme.

Either of Yoshihara et al. or Tanuma et al. teach antibodies specific for the human DNase-I-like enzyme.

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to have made additional antibodies specific for the DNase-I-like protein associated with fertility, guided by the disclosures of Yoshihara et al. or Tanuma et al., and to have used these in the methods of Ax et al. because one would have had an extremely reasonable expectation of success based on the teachings of McCauley et al., wherein the protein desired for detection in the methods of Ax et al. is identified as a DNase-I-like protein, and the teachings of Yoshihara et al. or Tanuma et al., wherein guidance for the elicitation of antibodies specific for the same or a closely related protein are provided. One would have been motivated to make and use any available antibody in the assay to detect the antigen bound thereby because Ax et al. teach that merely detecting the presence of the protein is indicative of increased fertility potential.

Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Baker et al. (US 6,482,626) disclose the sequence of the human LS-DNase (Figs. 1 and 2) and suggest making antibodies to the protein (col. 9).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James L. Grun, Ph.D., whose telephone number is (571) 272-0821. The examiner can normally be reached on weekdays from 9 a.m. to 5 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, SPE, can be contacted at (571) 272-0823.

The phone number for official facsimile transmitted communications to TC 1600, Group 1640, is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application, or requests to supply missing elements from Office communications, should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

James L. Grun, Ph.D.
September 19, 2006

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